

Clean Version

Please amend the paragraph at page 9, line 10 as follows:

– The invention relates to a pharmaceutical composition comprising i) ketotifen or an analog thereof and ii) a chemotherapeutic drug subject to multi-drug resistance by P-gp, preferably an anthracycline, more preferably doxorubicin or an analog thereof. The term subject to multi-drug resistance means that the chemotherapeutic drug's efficacy is reduced, or may become reduced, in a subject, tissue or cell because of clinical drug resistance associated with multi-drug resistance. For example, a chemotherapeutic drug subject to multi-drug resistance by P-gp includes anthracycline and doxorubicin or an analog thereof. A person skilled in the art can assess whether a chemotherapeutic drug is subject to multi-drug resistance by P-gp. For example, the chemotherapeutic drugs to be tested can be incubated with cells, such as P388/adr murine leukemia cells and normal P388 cells as a control. If there is reduced killing of the P388/adr murine leukemia cells as compared to the controls (e.g. normal P388 cells or chemotherapeutic drugs known not to be subject to multi-drug resistance) then the chemotherapeutic agent is subject to multi-drug resistance. In order to determine whether the multi-drug resistance is by P-gp the cells can be stained with a P-gp antibody, such as MRK-16, and the expression of P-gp can be compared to controls. A person skilled in the art will appreciate that other cell lines could be used, such as comparing the toxicity of the chemotherapeutic agent and P-gp staining in normal MCR-7 cells versus MCF-7/adr cells. --

Please amend the paragraph at page 10, line 4 as follows:

-- The pharmaceutical composition of the present invention is useful for treating cancer and reducing neoplasia and/or abnormal, uncontrollable cell growth and division. The pharmaceutical composition is also useful for i) circumventing, preventing, or treating multi-drug resistance in an animal and ii) preventing a chemotherapeutic drug subject to multi-drug resistance by P-gp, preferably anthracycline, more preferably doxorubicin or an analog thereof induced cardiac tissue damage in an animal. The pharmaceutical composition is also useful in preventing or treating multi-drug resistance in cancer cells, tumors or neoplasia. The anthracycline protective effects and reversal of MDR were unknown prior to this invention. --

Please amend the paragraph at page 10, line 19 as follows:

-- The invention also includes a method for treating cancer in an animal, comprising administering to the animal an effective amount of the pharmaceutical composition of the invention or the agents of the kit of the invention. The cancer can be a solid tumor, a hematological malignancy, or cells overexpressing P glycoprotein. --

Please amend the paragraph at page 11, line 17 as follows:

-- The invention also includes the use of the pharmaceutical compounds and compositions of the invention as a pharmaceutical substance for treating cancer in an animal, for i) preventing or treating multi-drug resistance in an animal or ii) preventing a chemotherapeutic drug subject to multi-drug resistance by P-gp induced cardiac tissue damage in an animal, for the preparation of a medicament for treatment of cancer, or for preventing or treating multi-drug resistance in cancer cells, tumors or neoplasia, preferably for the treatment of multi-drug resistance. --

Please amend the paragraph at page 12, line 1 as follows:

-- As mentioned above, one embodiment of the invention is a pharmaceutical composition for use in treating cancer. The invention also contemplates methods for treating cancer by administering compounds of the invention (for example, ketotifen and doxorubicin) to an animal. P-gp is found in a variety of leukemias and solid tumors [30]. The term cancer includes, without limitation, a solid tumor, a hematological malignancy or cells overexpressing P glycoprotein. The term cancer also includes any cancer including, without limitation, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer (such as carcinoma, ductal, lobular, and nipple), prostate cancer, non small cell lung cancer, Non-Hodgkin's lymphoma, multiple myeloma, leukemia (such as acute lymphocytic leukemia, chronic lymphocytic leukemia, acute myelogenous leukemia, and chronic myelogenous leukemia), brain cancer, neuroblastoma, and sarcomas. [32-36] In a preferred, example the cancer cell overexpresses P-glycoprotein. --